PATENT

Attorney Reference Number 11936.6US1
Application Number 09/739,406

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Weiyu Fan

Art Unit: 1616

Application No. 09/739,406

Filed: 12/18/2000

For: Chitosan and method of making chitosan

Examiner: Levy Neil

Date: 12/03/2004

CERTIFICATE OF MAILING

I hereby certify that this paper and the documents referred to as being attached or enclosed herewith are being deposited with the United States Postal Service on December 3, 2004, as First Class Mail in an envelope addressed to: MAIL STOP AF, COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450.

Paula DeGrandis
Attorney for Applicant

MAIL STOP AF
COMMISSIONER FOR PATENTS
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450

DECLARATION BY LAWRENCE E. FOSDICK PURSUANT TO 37 C.F.R § 1.132

I, Lawrence E. Fosdick, hereby declare as follows:

1. I currently am a Research Fellow/Chemistry Team Leader in the Acidulants business unit of Cargill, Inc., Eddyville, IA. I received a Ph.D. in Analytical Chemistry at the University of Georgia, Athens (1987) where my dissertation focused on microelectrode array and spectroelectrochemical flow sensors, including research into computer simulation of flow sensor response, electrode fabrication using microlithographic technology, and characterization of microelectrode arrays in flow cells. I also received a M.S. in Analytical Chemistry from University of Nebraska, Lincoln (1979) and a B.A. in Chemistry from Illinois Wesleyan University, Bloomington (1976). A copy of my *curriculum vitae* is attached hereto (Exhibit A).

2. I have reviewed the Office action dated August 3, 2004, concerning patent application No. 09/739,406. I also have reviewed the references cited therein.

3. The Examiner has asserted that "The selection of degree of deacetylation is shown as a result effective parameter chosen to obtain desired effect. As is the % in a composition is a matter of choice, depending upon [and] end use intended" (page 4, first full paragraph).

This statement, however, is not completely accurate. The ability to make various natural polymer products from biological material is significantly impacted by the biological material used as a source of the polymer. The cell wall structure of fungi is complex, containing many structures that are both chemically and physically bonded to each other and that are not present in the shells from crustaceans. Hence, it is not true that merely because a highly deacetylated chitosan can be made from shellfish it can also be made from fungi. This is especially true because of the bonding of glucans to the chitin in fungi cells walls.

4. The Examiner also asserted that "The viscosity and turbidity then follow as functions of the degree of deacytelation and concentration of the chitosan" (page 4, first full paragraph).

This statement is also not completely accurate. It is known by those of ordinary skill in the art that suspended and colloidal matter, such as insoluble glucans, cause turbidity (Standard Methods for the Examination of Water and Waste Water, 19th ed. 1995, edited by A. D. Eaton, page 2-8). Chitosan, when fully dissolved in solution, does not cause turbidity. The solubility is somewhat dependent on the degree of deacetylation, but the solubility was not exceeded in the instant invention specification. It was for this reason that turbidity was used to describe the chitosan containing material in the instant patent application.

More specifically, turbidity is an expression of the optical property that causes light to be scattered rather than absorbed or transmitted with no change in flux direction. Nephelometric turbidity is a method to measure the amount of light scattered by a sample compared to the amount of light scattered by a solid. Formazin polymer, chosen for its properties linking concentration and turbidity, is the most common material used to standardize instruments designed to measure turbidity.

5. To illustrate this point I performed the experiment described below.

A sample of chitosan prepared using the invention disclosed in U.S. patent application 09/739,406 was used in this study.

A 1% wt/wt chitosan solution in 1 % wt/wt aqueous acetic acid was prepared by:

1) Dissolving 6 g of glacial acetic acid in 588 g of deionized water

2) Dissolving 6 g of chitosan into the solution from Step 1

3) Mixing at room temperature for 1 hour to ensure full dissolution

A gel was also made that comprised glucans and chitosan from the glucan portion of the invention. The gel contained:

3.4 wt% total dry solids

75% of the solids were comprised of glucans

25% of the solids were comprised of chitosan

96.6 wt% water

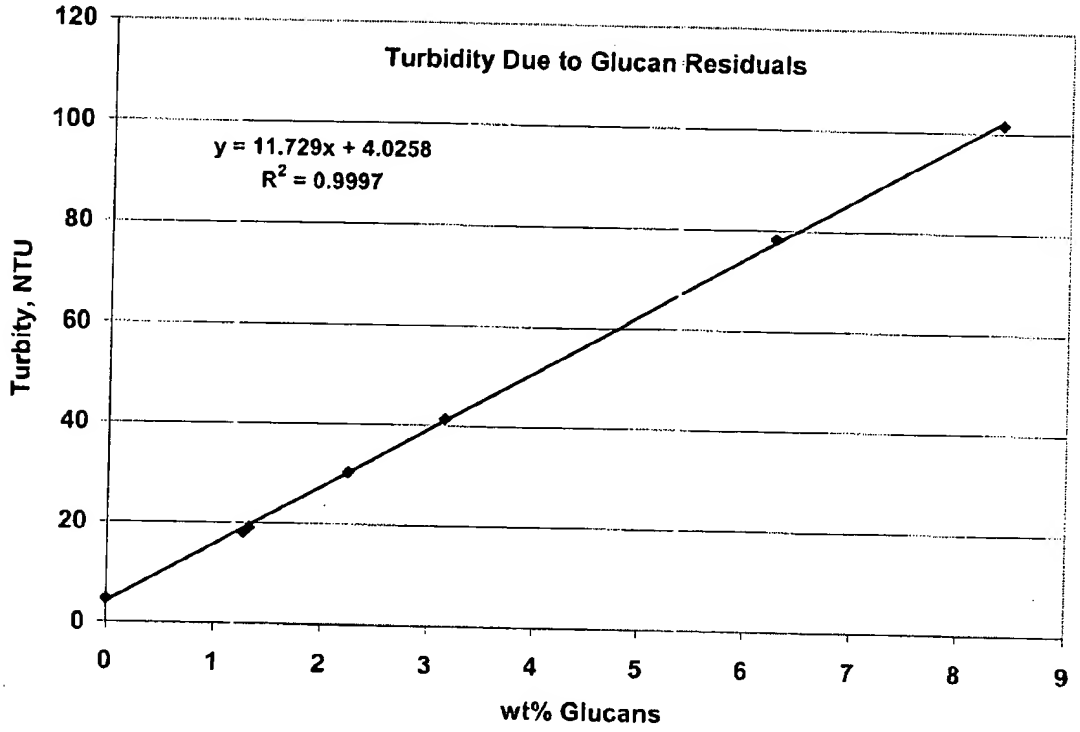
Aliquots of the glucan/chitosan gel were added to the 1% chitosan solution, then dispersed by mixing for 15 minutes on a mechanical shaker. The nephelometric turbidity of each sample was measured using a HACH turbidimeter (HACH Company, P.O. Box 389, Loveland, CO 80539-0389), with results reported as NTU (nephelometric turbidity units).

Table 1

g glucan/ chitosan gel	total g with 1% chitosan	% of solids as glucans	turbidity NTU
0	(blank)*	0	4.6
0.2192	41.3425	1.27	18.1
0.2662	48.3497	1.32	19.1
0.4208	44.6376	2.24	30.4
0.5520	41.3053	3.15	41.4
1.0201	37.2852	6.26	78.2
1.4831	39.7408	8.36	101.6

*1% chitosan with no added glucans for baseline turbidity

The results show that the measured turbidity increases linearly with respect to the percentage of the total solids present as glucans. The very low turbidity reported for the chitosan solution without added glucans indicates that the chitosan from the instant invention was essentially free of glucans or other insoluble matter.



6. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

By Lawrence E Fosdick
Lawrence E. Fosdick, Ph.D.

Date December 3, 2004

Lawrence E. Fosdick, Ph.D.

609 21st Avenue West, Oskaloosa, Iowa 52557
Work: (641) 969-3944 Home: (641) 673-3099

PROFESSIONAL SUCCESS FACTORS

- Demonstrated ability to synthesize ideas, coordinate efforts and interpret results to draw meaningful conclusions
- Accomplished in defining projects and identifying approaches to solutions that maximize return on investment
- Proficient in task and project prioritization, and resource utilization to achieve results that add value
- Skilled in coaching, creating learning opportunities for myself and coworkers to enhance relevant skills and job satisfaction

PROFESSIONAL EXPERIENCE

Research Fellow/Chemistry Leader, Acidulants R&D, Cargill, Inc., Eddyville, IA
Cargill Acidulants develops and produces products using large-scale fermentation technology.

1996 – present

- Recruited and coached chemists to maximize team effectiveness and job satisfaction
- Enhanced chemistry's value to Cargill by providing technical information in a timely manner to multiple Business Units
- Participated in and led teams drawn from multiple Cargill sites and BUs to better leverage resources within the Company, including international teams
- Participated in Acidulants strategic planning
- Participated in the development and launch of glucosamine from a non-shellfish source
- Collaborated with personnel from Cargill plants in process and analytical problem-solving
- Assisted in plant startup efforts for organic acid plants in North and South America, including technology transfers, pilot processes support, method development, and laboratory startup for citric acid, itaconic acid, lysine, erythritol, and glucosamine
- Active in intellectual property strategy and patenting
- Developed methods and trained team members to make measurements in fermentation, chemical modification, and process recovery samples
- Participated in methods evaluation and validation for regulatory compliance
- Served on AOAC expert review panel for glucosamine assay method

Sr. Research Chemist, Analytical Science Division, Hercules Incorporated, Wilmington, DE

1987 – 1996

- Analytical Technology Development Project Manager: seed money for new ideas: $200M budget which resulted in the development of several new and useful analytical techniques
- Member of Special Problems group, leading and participating in multidisciplinary analytical projects to support both product development and plant process issues
- Worked with research teams, processing plants, technical sales force, and customers to develop products and applications or solve challenges
- Led inorganic analysis group consisting of up to seven chemists and technicians
- Worked with FDA and EPA on regulatory issues and testing procedures
- Led effort to assess interferences in an EPA-required method from plant wastewater that threatened to close the plant. Developed evidence of interference and negotiated alternatives with state regulators

Sr. Applications Chemist, Electrochemistry Products Group, EG&G PARC, Princeton, NJ

1982 – 1984

- Provided electrochemistry support and coaching to sales force and customers
- Presented technical papers or training on electrochemistry at meetings and seminars in the United States and Europe
- Wrote technical application notes to provide information promoting product utility
- Developed advertisements and marketing brochures to promote electrochemistry techniques
- Championed a new computer interface for the premiere product line; provided key technical support for product development and successful launch

Analytical Chemist, Contract Management Team, Midwest Research Institute, Kansas City, MO

1979 – 1981

- Member of team in Saudi Arabia expanding and modernizing the Saudi Consumer Protection Department
- Worked with contractors from several countries to modify the building and utilities necessary for a successful laboratory operation
- Participated in food testing laboratory setup- instruments, methods, and training Saudi chemists
- Worked with WHO on regulatory issues, specifications, and methods

Analytical Chemist, Pharmaceutical Checker, Dorsey Laboratories, Lincoln, NE

1978 – 1979

- Tested raw materials and products in the Quality Assurance Lab using USP methods
- Monitored manufacturing and packaging for compliance with GMPs and FDA regulations

Research Chemist, Weber Marking Systems, Arlington Heights, IL

1976, and Summer '77.

- Developed duplicating stencil formulations, based on filmformer/plasticizer interactions
- Developed gel permeation chromatography for filmformers, plasticizers, and adhesives

AFFILIATIONS

AOAC Dietary Supplement Task Force member
Oskaloosa Library Board of Trustees member
Oskaloosa School District Talented and Gifted Advisory Committee member
American Chemical Society

EDUCATION

Ph.D., Analytical Chemistry, University of Georgia, Athens (1987)
Dissertation topics: Microelectrode array and spectroelectrochemical flow sensors, including research into computer simulation of flow sensor response, electrode fabrication using microlithographic technology, and characterization of microelectrode arrays in flow cells

M.S., Analytical Chemistry, University of Nebraska, Lincoln (1979)
Thesis topic: Sulfonyl Groups as Linking Agents for Chemically Modified Tin Oxide Semiconductor Electrodes

B.A., Chemistry, Illinois Wesleyan University, Bloomington (1976)

HONORS

American Chemical Society, Northeast Georgia Chapter, Outstanding Graduate Student of Chemistry, 1986
American Chemical Society, Analytical Graduate Research Fellowship, Honorable Mention, 1986
University of Georgia Chemistry Departmental Research Fellowship, 1985, 1984

PUBLICATIONS

B.D. Rogers, L.E. Fosdick, J.A. Bohlmann, "N-Acetyl-D-Glucosamine (NAG) Supplemented Food Products and Beverages", WO 2004/041199 A2, 2004

B.D. Rogers, L.E. Fosdick, J.A. Bohlmann, "Heat Pasteurized Liquids Containing Glucosamine", WO 2004/041198 A2, 2004

B.D. Rogers, L.E. Fosdick, J.A. Bohlmann, P.A. DeGrandis, "Multiple Component Food Product Useful for Delivering Glucosamine and/or N-Aectylglucosamine", WO 2004/040997 A2, 2004

L.E. Fosdick, J.A. Bohlmann, J.R. Trinkle, B.L. Ray, "Glucosamine and Method of Making Glucosamine from Fungal Biomass", US 20040077055 A1, 2004

K.R. Anderson, A. Esser, L.E. Fosdick, K. Hwang, N. Mahr, J.T. McDonald, D.S. Sivasligil, A. Stange, S. Veelaert, M. Wendker, "Compositions Suitable as Additives in the Paper Industry, Preparation; Use; and Paper Comprising Such", US 6,710,175, 2004

L.E. Fosdick, T.W. Bauer, J.A. Bohlmann, K. Hwang, B.D. Rogers, "Glucosamine Organic Acid Adducts", WO 03/49696 A2, 2003

L.E. Fosdick and J.L. Anderson, "Spectroelectrochemical Response and Flow Hydrodynamics in Thin-Layer Flow Detectors with Long Optical Path Lengths and Fiber Optic or Slab Waveguide Coupling", *Anal. Chem.*, 1988, 60, 163-168

L.E. Fosdick and J.L. Anderson, "Spectroelectrochemical Response and Optical Geometry of Thin-Layer Flow Detectors with Long Optical Path Lengths: Theory", *Anal. Chem.*, 1988, 60, 156-162

L.E. Fosdick, "Reference Library: A Keyword-Based Article Storage and Retrieval System", *80-Micro,* 1987, No. 84, 48-57

L.E. Fosdick, T.A. Baginski, R.C. Jaeger, and J.L. Anderson, "Amperometric Response of Microlithographically Fabricated Microelectrode Array Flow Sensors", *Anal. Chem.*, 1986, 58, 2750-2756

L.E. Fosdick and J.L. Anderson, "Optimization of Microelectrode Array Geometry in a Rectangular Flow Channel Detector", *Anal. Chem.*, 1986, 58, 2481-2485

A.L. Cordry, L.E. Fosdick, and R.C. Larson, "Sulfonyl Groups as Linking Agents for Chemical Modification of Electrodes", *J. Electroanal. Chem.*, 1985, 186, 87-97

L.E. Fosdick, "Electroless Plating Bath Analysis Using Voltammetric Techniques", Proceedings of the Second Electroless Plating Symposium, American Electroplaters Society, Orlando, Florida, Feb 1984, paper D

L.E. Fosdick and R. Pike, "Polarographic Determination of Kjeldahl Nitrogen", *J. AOAC*, 1982, 65, 178-180